

ABSTRACTS

(The abstracts are divided into the following sections: syphilis (general); penicillin in syphilis; gonorrhœa; general. After each subsection of abstracts follows a list of articles that have been noted but not abstracted.)

SYPHILIS (GENERAL)

Carriers of Syphilis. (Les porteurs de germes syphilitiques.) BESSEMANS, A., and VERCOULLIE, J. (1946). *Brux. méd.*, 26, 1133.

Treponema pallidum can live as a saprophyte on the body surface for some time before it accomplishes penetration, and this may account for certain cases with an extraordinarily long incubation period. People with serological evidence of syphilis but with no clinical signs of disease have often been proved contagious. *T. pallidum* has been demonstrated in cervical secretions of women showing no sign of disease but who have been in contact with men with florid syphilis. The organism has also been found in the lymph nodes of latent syphilitics.

Cases of contamination by syphilitics showing no surface lesions or serological evidence of disease have often been described—as by the bite of a patient with general paresis (positive evidence in the cerebrospinal fluid). People incubating syphilis can spread the disease. [This is a most important point which is often insufficiently stressed.] The blood may be highly contagious at any stage, and this bears no relation to the reaction of the serum.

Three cases are cited: (1) A woman was living with a man who was found accidentally to have a positive Wassermann reaction. The woman gave no history and showed no signs of syphilis, and serum tests were negative. She was accused of being the source of infection in the case of another man with whom she had intercourse 5 weeks before the start of investigations in her case, and who developed a chancre 16 days after coitus. (2) A prostitute, under supervision every fortnight over 3 years, had been in hospital 4 times in this period; fortnightly serum tests over several months gave negative results, free from any evidence of syphilis. She was accused of infecting a man with syphilis, coitus having taken place several days before her last (negative) serum test was made. (3) A prostitute was under fortnightly control with frequent serum tests over 3 years and 4 months, showing no evidence of syphilis. Three times in this period, at intervals of 4 and 15 months, she was accused of having transmitted syphilis to men. The infected men in these cases all denied the possibility of any other source of contamination. In case (2) the woman still showed no evidence of disease some

months later. Seminal transmission of *T. pallidum* is suggested as the most likely method in case (1).

The absence of syphilis in these cases may be explained by a natural local immunity or by an immunity acquired by repeated contact with *T. pallidum*. [Janet (*Diagnostic et Traitement de la Blennorrhagie*) suggested that prostitutes, after many attacks of gonorrhœa, eventually develop a certain immunity.] Rabbits and mice were inoculated with cervical secretions from these women, but no syphilomata developed in the rabbits, and lymph node transfers (4 to 5 months later) from both the rabbits and the mice produced no lesions in rabbit testicles. These experiments suggest that the infecting agent had disappeared from the genital tract between 1 and 2 months after the suspect coitus.

Other articles are cited in which persistence of *T. pallidum* in the vaginal or other secretions for varying lengths of time has been noted. The authors conclude that there is a strong probability that *T. pallidum* may, in certain women, be a true saprophyte and that such women may simply act as vectors.

[Although there is no reason to deny the possibility of the existence of carriers of syphilis, the cases cited are not convincing. The article is interesting in its exposition of the infectivity of syphilis at various stages and in various ways.]

James Marshall

Physicopyrexia and the Biologic Healing of Early and Late Syphilis of the Rabbit. BESSEMANS, A., and DENOO, A. (1946). *Arch. phys. Med.*, 27, 547.

An investigation was carried out on rabbits, 154 of which were infected with the Ghent strain of syphilis. The decision was taken to combine chemotherapy and artificial pyrexia, since it seemed possible to obtain better results in this way than with either method separately. In some animals the disease had lasted 4 months (early cases), in others from 6 to 16 months (late cases). Three groups were chosen: one was treated by arsphenamine only, the second by artificial pyrexia only, and the third by both together. The arsphenamine was given in the form of a 10% solution of "solusalvarsan," 3 intramuscular injections of 0.25 or 0.5 ml. per kilo of body weight being employed at 3- or 8-day intervals. Artificial pyrexia was induced with the rabbit wholly inside a wooden cabinet, the air in which was heated

electrically and kept moving by a fan. The inductortherm cable was wound round the outside of the incubator, the rabbit thus lying within the electromagnetic field. In other cases the rabbits' heads were allowed to protrude from the incubator. These treatments were given at 3- to 8-day intervals. Temperatures of 42° C. were attained for 30 to 60 minutes and 41° C. for 2 hours. The rabbits in the third group were treated by both arsphenamine and pyrexia, the latter being induced either on the same day as, or on the day after, the injection. In all, 92 rabbits survived treatment.

Three tests of cure were employed: (1) testicular implantation into a normal rabbit of popliteal lymph nodes from an infected rabbit; (2) transplantation of an emulsion made from various organs of the infected rabbit; (3) re-inoculation of a previously infected rabbit with a homologous strain of *Treponema*, to determine whether a fresh syphiloma formed. Evidence of re-infection suggested previous complete cure. Great stringency and thoroughness were shown in evaluating the results; the types of reaction and the temperatures reached at various parts of the body are explained diagrammatically. The percentage cured was as follows:

	Arsphenamine alone	Pyrexia alone	Combined treatment
Early cases ..	60%	54%	100%
Late cases ..	25%	27%	83%

Injections acted best when given just before the pyrexia, over 95% of the animals being cured as opposed to 75% when the injection was given afterwards. The authors attribute this success with the combined treatment to pyrexial stimulation of the natural defences, and show reason for hoping that combined therapy in human syphilis will bring about actual healing rather than mere masking of symptoms.

J. H. Cyriax

The Value of the Quantitatively Standardized Complement Fixation Test in the Diagnosis and Treatment of Early Syphilis. MAILLARD, E. R., and ORZEL, A. *Amer. J. Syph.*, 30, 490.

The results are given of quantitative complement-fixation tests in 693 patients with early syphilis treated with penicillin. Specimens were taken immediately before and after treatment, and then at weekly and, later, at monthly intervals. Over a period of 10 months 4,883 specimens were tested. The 693 patients included 196 with primary and 497 with secondary syphilis; 44 of the primary cases gave negative reactions before treatment, but 17 of these showed a weak reaction after treatment. Of the primary cases 50% showed no reaction with lesions less than a week old, 25% with lesions to 2 weeks old, and 5% with lesions from 2 weeks old; no negative reactions were obtained when lesions had been present for

4 weeks. Of the patients with primary syphilis 83% had titres of less than 50, whilst 93% of the secondary cases had titres of over 50. The highest titre in a primary case was 150 and in a secondary case 630. Of the 693 patients 325 were followed up for 3 to 10 months; 211 (87 primary and 124 secondary) showed a uniform drop in titre—when the initial titre was between 10 and 50, 3 months were required for the titre to fall to 8; when it was greater than 50, 3 to 6 months were required. The relapse rate was high since the dosage of penicillin varied from 60,000 to 600,000 units. Relapses occurred in 20% of the primary and 43% of the secondary cases, and 85% of relapses appeared within 6 months. Muco-cutaneous lesions were found in 70% of patients showing serological relapse. It is concluded that this quantitatively standardized complement-fixation test is of great value in diagnosis, prognosis, and the control of treatment.

[The technique of this test is complicated and requires first-class pathological facilities. When the test is simplified it may be suitable for general use.]

T. E. Osmond

The Treatment with Massive Arsenotherapy of Early Syphilis Complicated by Pregnancy. CURTIS, A. C., and MORROW, G. (1946). *Amer. J. Obstet. Gynaec.*, 52, 284.

It is claimed that massive arsenical therapy offers a rapid and efficient method of treating syphilis in pregnancy. The results of Jeans (*Amer. J. Syph., Gon. Vener. Dis.*, 1919, 3, 114) and of Marshall (*J. Amer. med. Ass.*, 1934, 102, 503) show the high incidence of stillbirth, abortion, and infant mortality when pregnant women with latent syphilis are untreated. The results of Marshall, McKelvey, and Turner (*J. Amer. med. Ass.*, 1934, 102, 503) show that the foetal prognosis is proportional to the adequacy of antenatal anti-syphilitic treatment. The good results of Sudusk and Shaffer (*Yale J. Biol. Med.*, 1942, 14, 34), Rattner (*Amer. J. Obstet. Gynaec.*, 1943, 46, 255) and others with massive arsenotherapy by the 5-day drip method are recorded. The authors give their own results in 30 cases treated by the total injection of 1,200 mg. of mapharside with 260 mg. of bismuth. They then describe the treatment of 10 cases by a modified technique, in which a total of 1,080 mg. of mapharside in 5% glucose was given intravenously by daily injections, with the associated administration of 4 doses of 130 mg. of bismuth subsalicylate in oil intramuscularly. Liver and renal function were tested, and a blood count was made before treatment was begun. Neither abortions nor stillbirths occurred in this series. The fallacies of the testing of cord blood, of the Wassermann test, and of examination of the placenta, and the value of dark-ground examination of serum from the umbilical vein or infant's skin, are emphasized.

J. Stallworthy

Clinical Surgery and the Serodiagnosis of Syphilis. (Clinica y serodiagnostico de la sifilis.) GARRIDO QUINTANA, F. (1946). *Actualid. méd.*, 22, 516.

Modern Treatment of Syphilis. THOMAS, E. W. (1946). *Amer. J. publ. Hlth.*, 36, 1002.

Results of Rapid Treatment of Early Syphilis. HELLER, J. R. (1946). *J. Amer. med. Ass.*, 132, 258.

Syphilis in Army Separates. ROSENTHAL, T., and SOBEL, N. (1946). *N.Y. St. J. Med.*, 46, 2042.

Should Cardiovascular Syphilis be treated Antisyphilitically? (Bør syfilitiske Hjerte-Karlidelser behandles antisyfilitisk?) BUCH, H. (1946). *Ugeskr. for Læg.*, 108, 1106.

The Kline Reaction for the Serodiagnosis of Syphilis. (Sobre la reacción de Kline para el serodiagnóstico de la sifilis.) CARGO VILLEGAS, A., and GARRIDO BLANCO, A. (1946). *Laboratorio*, 2, 221.

A Case of Syphilitic Meningo-Encephalomyelitis. (Su di un caso di meningo-encefalo-mielite iuetica.) BUTTARO, C. A. (1946). *Rass. int. Clin. Terap.*, 26, 297.

Tertiary Syphilis of the Pharynx. (Fall av tertiärlues i avalget.) BRANTEFORS, G. (1946). *Nord. Med.*, 31, 2065.

Two Anniversaries in the History of Syphilis Research. (Zwei Gedenktage der Geschichte der Syphilisforschung.) HOFFMANN, M. (1946). *Arch. Derm. Syph., Berlin*, 186, 93.

Intolerance and Effects of Arsphenamines in Syphilis. (Intoleranz und Wirkung der Arsenbenzole bei der Syphilis.) TRUFFI, M. (1946). *Arch. Derm. Syph., Berlin*, 186, 54.

Syphilis in Pregnancy. (Sifilis en el embarazo.) MESA RAMOS, J. D. (1946). *Bol. Soc. cubana Derm. Sif.*, 3, 97.

A case of Syphilis of the Stomach. (Bir mide sifilisi vak'asi.) BILHAN, N. (1946). *Turk Tip Cem. Mec.*, 12, 201.

Anti-syphilis Treatment. (Die antiluetische Kur.) ROTTER, H. (1946). *Wien. klin. Wschr.*, 58, 631.

Today's Treatment of Syphilis. O'LEARY, P. A., and KIERLAND, R. R. (1946). *J. Amer. med. Ass.*, 132, 430.

SYPHILIS (Kahn Reactions)

The Verification of Kahn Reactions. (Le reazione di verifica della reazioni di Kahn.) DE FILIPPIS, V. (1946). *G. Clin. med.*, 27, 524.

Simplification of the Kahn Reaction. (Simplificación de la reacción de Kahn.) LAZO GARCIA, S. (1946). *Hispania med.*, 3, 345.

PENICILLIN IN SYPHILIS

The Effect of the Method of Administration on the Therapeutic Efficacy of Sodium Penicillin in Experimental Syphilis. EAGLE, H., MAGNUSON, H. J., and FLEISCHMANN, R. (1946). *Bull. Johns Hopk. Hosp.*, 79.

The curative dose of sodium penicillin in rabbit syphilis has been found to be affected by the number of injections given: the greater the number, the less the total amount of penicillin needed for a cure, though no appreciable difference is noted if these injections are given 4-hourly or twice or once daily.

Nearly 350 rabbits were inoculated intratesticularly with Nichol's strain of *Treponema pallidum*, and treatment was started after the development of testicular syphilomata 5 to 7 weeks later. Thirteen different schedules, with intervals between injections of 15 minutes to 4 days, the number of injections varying from 4 to 50 and the duration of treatment from 3 hours to 16 days, were used. On each schedule from 3 to 9 rabbits were treated with commercial penicillin at each of 3-7 dosage levels. Cases where spirochaetes were still present 72 hours after treatment, or where they subsequently reappeared, were regarded as failures.

In rabbits injected at 4-hourly intervals, as the number of injections increased from 8 to 20 to 50, and the duration of treatment from 32 hours to 8 days, the total curative dose (C.D.₅₀) fell from 80,000 to 1,600 units per kilo respectively. Similarly, in rabbits injected twice daily, merely doubling the number of injections from 8 to 16 and the duration of treatment from 4 days to 8 days, reduced the total curative dose (C.D.₅₀) from 30,000 to 1,700 units per kilo. When the number of injections was kept constant, and only the interval between them varied, the curative dose (C.D.₅₀) was similar whether injections were given every 4 hours, twice daily, or once daily (4,000, 1,770, and 4,000 units per kilo). On the other hand, when the injections were given so frequently as to produce cumulative effects on the blood penicillin level, therapeutic efficacy was paradoxically reduced. Thus the curative doses of sodium penicillin given in 16 injections at 4-hourly, 2-hourly, and 1-hourly intervals were 4,000, 32,000, and 64,000-units per kilo respectively. When the total duration of treatment was fixed, and the number of injections varied, the therapeutic efficacy of penicillin increased with the frequency of injection. In rabbits treated over a period of 4 days, as the frequency of injection was changed from once daily to twice daily to every 4 hours, and the number of injections correspondingly increased from 4 to 8 to 20, the total curative dose (C.D.₅₀) fell from 50,000 to 20,000 to 1,600 units per kilo. Low concentrations acting over a long period of time were more effective than high concentrations over a short period. For an equal number of injections, treatments given once daily were as effective as injections every 4 hours with a suggestion of an optimum interval of 8-12 hours.

With mapharside the drug is bound by the organism in competition with the tissues, and the single exposure to high concentration is as effective as repeated exposures to a lesser concentration. Penicillin, on the other hand, is effective only so long as it is present in the surrounding fluid, though it is apparent that the actual amount required to be present is very low. Thus, 50 4-hourly injections of only 7 units per kilo over 8·3 days were as effective as 8 4-hourly injections of 6,000 units over 1·3 days; similarly in animals treated twice daily, if the duration of treatment is reduced to 8 from 16 injections, the total curative dose (C.D.₅₀) for injection is increased from 110 to 3,750 units per kilo. The spirochaeticidal effects of penicillin *in vitro* have been noted in concentrations as low as 0·01 unit per c.cm. In rabbits treated by 50 4-hourly injections of 10 units per kilo a C.D.₅₀ was obtained when penicillin was never demonstrable in the blood.

Methods of administration which yield blood levels above 0·01–0·2 unit per c.cm. waste a large part of the potential activity of the penicillin, and treatment schedules should minimize wasteful peaks in the blood. This can be achieved either by repeated small doses at short intervals, continuous intravenous or intramuscular drip, or by using a penicillin in oil-beeswax delayed-absorption method; though by the latter only the number of injections, and not the time duration of treatment, should be reduced. Milligramme for milligramme, penicillin in rabbit syphilis is between 10 and 20 times as effective as mapharside, though in the human subject it is apparently only 2 to 4 times as effective, and with both drugs rabbit syphilis is easier to cure than the human form. If it is desired to improve on results by increasing the dose of penicillin, then double the dose given over the same time is not likely to be nearly so effective as if double the dose were spread over double the time.

R. R. Willcox

The Effect of the Sodium Salts of Crystalline Penicillin G, Crystalline Penicillin X, and Commercial Penicillins on Dark-field Positive Lesions of Syphilis. OLANSKY, S., and PUTNAM, L. E. (1946). *J. vener. Dis. Inform.*, 27, 178.

To date there is evidence that there are at least four penicillins in commercial penicillin. It has been shown that penicillin X is more effective than commercial penicillin in the treatment of gonorrhoea. Of 128 cases, 87·5% showed clinical cures after single injections of 25,000 units of penicillin X, as compared with only 64% of 68 cases with the same amount of commercial penicillin. The possibility therefore exists of a penicillin that is selective for the gonococcus and will not at the same time mask a concomitant infection with syphilis.

In this study the effectiveness of single doses of 50,000 units of two crystalline penicillins (G and X) was contrasted with that of several commercial penicillins as to the rate of disappearance of *Treponema pallidum* in patients suffering from

dark-field-positive primary syphilis. Of 10 patients treated with crystalline penicillin G, 6 had negative dark-field tests 8 hours after treatment, 2 at 10 hours, and 2 at 14 hours (average, 9·6 hours); 3 showed Herxheimer reactions and 2 had gonorrhoea which cleared promptly. Of 10 patients treated with crystalline penicillin X, only 2 were negative on dark-field testing at 14 hours, and 8 still had active treponemata in the lesions 24 hours after the injections. Both the successful cases showed Herxheimer reactions, and 6 also had gonorrhoea which cleared rapidly. Of 10 patients treated with a commercial penicillin G, 1 became negative at 12 hours, 4 at 14 hours, and 5 at 16 hours (average, 14·8 hours); 2 showed Herxheimer reactions. Of another group treated with commercial penicillin of predominantly G plus 16–18% X, 3 had negative tests at 16 hours, 4 at 18 hours, and 3 at 24 hours (average, 19·2 hours). There was one Herxheimer reaction in this series. Of 10 patients treated with a commercial penicillin containing 70% X, 7 were negative at 24 hours while 3 were still positive at that time. No Herxheimer reactions occurred in this group.

All patients showing Herxheimer reactions became dark-field-negative more quickly than others in each group. This may mean either that the Herxheimer is a manifestation of favourable response or that the associated fever was a contributory factor. It was thus noted that crystalline G was at least as effective as several commercial penicillins, and that X was less effective than G. There was no indication that any of the products so far tested might not mask a syphilitic infection.

R. R. Willcox

The Therapeutic Effectiveness of Relatively Crude Commercial Penicillin in Early and Late Rabbit Syphilis. FLEMING, W. L., and WOLF, M. H. (1946). *Amer. J. Syph.*, 30, 468.

Experiments were undertaken to discover the minimum curative doses of penicillin in early and late rabbit syphilis. The same batch of penicillin was used throughout; it contained 293 units per mg., 115,000 units per ampoule, and 25% of factor X. The rabbits were divided into two groups, each of 50, and given varying dosages of penicillin 6 weeks (early) and 6 months (late) after infection. The total dosages were 500, 1,000, 2,000, 4,000, and 8,000 units per kilo given in equal fractions every 3 hours for 32 doses. Proof of cure consisted of surveillance for recurrent lesions, and lymph node transfers after 6 to 8 weeks and after 6 months. In early syphilis the CD₅₀ (dose required to cure 50% of animals) was 1,100 units per kilo, and the CD₉₅ over 2,000 units; in late syphilis the figures were 500 and over 2,000 units respectively. The amount of penicillin required to cure late rabbit syphilis was less than that required to cure early lesions. The experiment was complicated by the fact that 2 rabbits developed keratitis but gave negative lymph-node transfers; this does not affect the conclusions drawn.

T. E. Osmond

The Rapid Treatment of Early Syphilis with the Combined Use of Penicillin and Mapharsen. BUNDESEN, H. N., CRAIG, R. M., SCHWEMLEIN, G. X., BARTON, R. L., and BAUER, T. J. (1946). *Amer. J. Syph.*, 30, 475.

Twelve white and 36 coloured males and 12 white and 47 coloured females (107 patients) with lesions of syphilis positive on dark-ground examination were treated by 60 intramuscular injections, each of 5,000 units of penicillin, given every 3 hours (total 300,000 units), together with a daily intravenous injection of 40 mg. of mapharsen (total 320 mg.), and were observed for 18 months.

The average number of days required for reversal of serum reaction was 47.6 for primary, 95.0 for secondary, and 248.0 for relapsing cases. Thirty-four patients were considered treatment failures; these included 10 cases of relapsing secondary syphilis, 3 of primary lesions progressing to the secondary stage, 11 relapses as judged serologically, 7 resistant cases, 1 recurrence with neuro-syphilis, and 2 possible re-infections, details of which are given. Primary fever (presumably Herxheimer reactions) occurred in 76 patients, and secondary fever in 59. The authors conclude that the amount of treatment given in this series is inadequate.

[This trial was carried out in the first 3 months of 1944; recent experience has shown that when 8 times as much penicillin and the same amount of mapharsen are employed, relapses still occur.]

T. E. Osmond

Penicillin by Mouth in the Treatment of Late Cutaneous Syphilis. WALLACE, E., and PAUL, W. D. (1946). *Amer. J. Syph.*, 30, 480.

A woman, aged 52, had scattered, discrete, dull red nodules about 4 mm. in diameter on the chin, and over the left scapular region there was an extensive lesion with gyrate outlines and a tendency to central clearing and peripheral spread, the border showing nodules similar to those on the chin. Biopsy revealed round cells, plasma cells, and epithelioid cells about the blood vessels in the sub-papillary layer; the endothelium of the vessels was thickened and disorganized; the deeper infiltrate showed epithelioid cells and an occasional giant cell. Kolmer, Kahn, and Kline tests of the blood were positive, and the Kahn titre was 240 units; cerebrospinal fluid tests were negative. The patient was given 7,800,000 units of penicillin over 10 days—that is, 100,000 units combined with 2.5 g. dihydroxyaminoacetate every 3 hours. The lesions showed continued regression 2 and 5 weeks after treatment. Illustrations show the lesions and biopsies before and after treatment. [It would have been interesting to know the effect of this treatment on the blood reactions.]

T. E. Osmond

The Treatment of Early Syphilis (in Africans) with Penicillin Sodium. COCHRANE, G. C. (1946). *E. Afr. med. J.*, 23, 287.

The amount of penicillin administered was 2.4 mega units in 3-hourly injections over 7½ days.

As a rule, owing to the prevalence of positive serological tests due to yaws, no case was diagnosed as early syphilis unless a positive dark-field test could be obtained. Treponemata were absent from the lesions between 6 and 24 (average 14) hours after the onset of treatment, and the average stay in hospital was 10 days. In contrast to Europeans, over 50% of whom experienced Herxheimer reactions, the incidence of such reactions in the African was negligible (0.09%), and all these were pyrexial responses in cases of secondary syphilis. No cases of urticaria were seen.

Clinical and serological relapse-reinfections were under 0.6%, though the total number treated and the period of observation are not stated. Of 112 sero-positive dark-field-positive cases the percentages becoming sero-negative each month from 1 to 6 months were 1.8, 47.5, 56.25, 78, 87, and 98, respectively. Intercurrent infections, such as smallpox, relapsing fever, and other tropical diseases, may produce a temporary elevation in the titre of the quantitative Kahn, which in some cases may be mistaken for a serological relapse.

R. R. Willcox

Preliminary Results in Penicillin Treatment of Primary and Secondary Syphilis. (Premiers résultats du traitement de la syphilis primo-secondaire par la cure unique de pénicilline.) VANSTEEN-ACKER, G. (1946). *Rev. méd. Liège*, 1, 207.

Penicillin Treatment of Syphilis. (La pénicilline dans le traitement de la syphilis: revue de travaux consacrés à cette question.) BEESON, M. B. B. (1946). *Ann. Derm. Syph., Paris*, 6, 395.

Toxic Effects of Penicillin Treatment in Pregnant Women. (In English.) GARCIA-BIRD, J. (1946). *Bol. Assoc. med. P. Rico*, 38, 220.

Penicillin Treatment of Syphilis. (Over de behandeling van syphilis met penicilline.) DE BERGH, J. (1946). *Ned. Tijdschr. Geneesk.*, 90, 1672.

Penicillin in the Treatment of Syphilis. (La pénicilline dans le traitement de la syphilis.) BOUVIER, J. B. (1946). *Paris med.*, 36, 554.

The Place of Penicillin in the Treatment of Syphilis. SHEPPE, W. M. (1946). *W. Va. med. J.*, 42, 217.

The Present Status of Penicillin in the Treatment of Syphilis. REQUE, P. G., and GALLOWAY, J. L. (1946). *N.C. med. J.*, 7, 469.

Penicillin Therapy of Early Syphilis. STERN, F. (1946). *Acta med. orient.*, 5, 273.

GONORRHOEA

Oral Penicillin Treatment of Gonorrhoea. COHN, A., KORNBLITH, B. A., and GRUNSTEIN, I. (1946). *Amer. J. Syph.*, 30, 485.

The authors investigated the effect of penicillin given by mouth on gonorrhoea. Blood-serum levels after a single oral dose of 50,000 units varied from 0.03 to 0.25 unit per ml. (average 0.08 per ml.) after half an hour and from 0.015 to 0.125 (average 0.05 unit per ml.) after an hour. When the single dose was 150,000 units the average levels were 0.52 and 0.029 unit respectively. Tests of cure included four lots of smears and cultures over a period of 3 weeks. For the experiment tablets containing calcium penicillin buffered with magnesium oxide and co-precipitated aluminium hydroxide and calcium carbonate were used. *Group I*: 13 men and 5 women received 3 doses, each of 150,000 units, at 2-hourly intervals; 10 men and 3 women were cured and 3 men and 2 women were not. *Group II*: 3 men and 11 women received 5 doses, each of 60,000 units, at 2-hourly intervals; 2 men and 8 women were cured. *Group III*: 18 men and 11 women received 5 doses, each of 120,000 units, at 2-hourly intervals; 12 men and 9 women were cured. *Group IV*: 40 men and 10 women received an initial dose of 150,000 units, followed by 50,000 units hourly for 6 doses and 150,000 units at the seventh hour; 36 men and all 10 women were cured. It appears that the time-dose ratio is important, hourly administration being necessary in order to obtain the best results, represented by a cure rate of about 90%. It is concluded that: (1) by mouth about four times as much penicillin as is given in a single injection intramuscularly in water-in-oil emulsion is required to obtain cure; (2) the effect of oral penicillin may be minimized by irregular self-medication, which may lead to sensitization and resistance; and (3) oral penicillin may mask a concurrent syphilitic infection.

[In view of the fact that gonorrhoea is usually more difficult to cure in women than in men it is of interest to note that in Group IV all 10 women were cured, but only 36 out of 40 men. In the whole series the percentages of cures in men and women were almost equal.]

T. E. Osmond

Penicillin for Gonorrhoea in the Female. MASCALL, W. N. (1946). *Lancet*, 2, 712.

Attention is drawn to the dangers of false optimism created by publicity given to reports of the efficacy of penicillin in treating infection. The limitations of penicillin therapy for gonorrhoea are discussed in a detailed report of this form of treatment in 39 consecutive patients at the L.C.C. (Whitechapel) Clinic. In 18 of the women penicillin failed to control the infection, and an additional 16 are regarded as probable failures. Women suffering from gonorrhoea alone were treated according to one of three schedules: (1) Five 2-hourly injections of 30,000 or of 60,000

units in aqueous solution; (2) a single injection of 200,000 units in aqueous solution; (3) a single injection of 150,000 or of 200,000 units in arachis oil and beeswax. There were 16 failures in this group of 24 cases. Gonococcal vulvo-vaginitis proved refractory to penicillin in the 3 children so treated. One of these cases relapsed after 150,000 and 300,000 units in divided doses had been given, and again after a single injection of 250,000 units in arachis oil and beeswax. Twelve patients also had syphilis, and were therefore treated with a total of 2,400,000 units—40,000 units 3-hourly by day and by night—and yet gonococci were subsequently found in 5 of them. The author suggests that the lack of success in gonorrhoea, even after a dosage as high as 2,400,000 units has been given, indicates the possibility that some strains of gonococci are naturally resistant or have acquired resistance.

V. E. Lloyd

Penicillin Treatment of Acute Gonorrhoea and its Complications, and Early Syphilis (in Africans) as Practised in the East Africa Command. COCHRANE, G. C. (1946). *E. Afr. med. J.*, 23, 285.

Treatment of gonorrhoea with penicillin was introduced into the East African Command in February, 1945. The dose employed was 100,000 units of sodium penicillin given in 5 3-hourly injections of 20,000 units dissolved in 1 c.cm. of distilled water. Response was rapid, gonococci being absent from the smears within 3 hours in 50% and within 6 hours in 80% of cases. In spite of this the average stay in hospital was 4 days, at the end of which time if the urine was still hazy a specimen was examined to exclude bilharzial infection, and if the urethral discharge persisted a dark-field test was performed for *Trichomonas hominis*. Relapses were infrequent, and there were no failures or toxic effects. Good results were also reported with the complications of epididymitis, prostatitis, and gonococcal ophthalmia. Tests of cure, including a Kahn test, were done after 3 months; all tests were satisfactory in uncomplicated cases, but the number of such cases actually treated is not stated.

[Though mention is made of the possibility of a delayed or masked syphilitic infection, apparently no further blood tests were done after 3 months.]

R. R. Willcox

Importance of the Gonococcal Strain in Resistance to Sulphonamides. (Sull'importanza del ceppo gonococcico nel fenomeno della sulfonamido-resistenza.) MIDANA, A. (1946). *Dermosifilografia*, 169.

The author states that at least 90% of fresh cases of gonorrhoea are now sulphonamide-resistant, and suggests that naturally-resistant strains of gonococci, as opposed to strains with an acquired resistance, are partly responsible for present-day infections. He reports 6 cases of fresh infection.

observed in 1943, when the proportion of resistant cases was relatively small. These were infected from the same source, which itself presented a sulphonamide resistant infection. Three of the cases were infected in parallel and 3 in series, but in all the infection was sulphonamide-resistant. In quoting work by Crosti on the passage of strains with an acquired resistance in man, the author implies that a naturally resistant strain caused the infection in the 6 cases reported, since in these cases the characteristic of sulphonamide resistance remained constant on transmission.

H. M. Adam

Masking of Early Syphilis by Penicillin Therapy in Gonorrhoea. FROMER, S., CUTLER, J. C., and LEVITAN, S. (1946). *J. vener. Dis. Inform.*, 27, 174.

The possibility that the relatively small dose of penicillin employed in the treatment of gonorrhoea might mask a previously or simultaneously acquired syphilitic infection has always been borne in mind. It is already appreciated that fevers and chills are rare during the penicillin treatment of gonorrhoea and that when such reactions are experienced they are strongly suggestive of an additional infection with syphilis. Such a patient may develop a primary sore in the ordinary way, or this stage may be missed and one or more of the signs of secondary syphilis may appear in a usual or attenuated form. Perhaps a positive serological test may be the only sign, and the incubation period, too, may be prolonged.

Of 1,000 patients suffering from early syphilis, 66 had received penicillin treatment for gonorrhoea within the previous 4 months. Of these, 18 had Herxheimer-like reactions at the time the penicillin was administered. It is postulated that, as the incubation period of gonorrhoea may vary between 7 and 30 days, and that of syphilis between 7 days and 4 months, combinations of long and short incubation periods of these two diseases may explain why some patients get febrile reactions and others do not. Thus, if the syphilis is contracted before the gonorrhoea, or if a long incubation period for gonorrhoea is combined with a short incubation period for syphilis, the patient would be highly parasitized and therefore liable to give a febrile reaction when the treponemata were killed by penicillin. On the other hand if the incubation period of the gonorrhoea is short and that of the syphilis long, the patient, being less highly parasitized, is less likely to show a Herxheimer reaction.

Three cases are quoted in support of this thesis. One patient showing a febrile reaction had a history indicating that the syphilis was contracted before the gonorrhoea, while one with and one without a febrile reaction were assumed to have acquired the two diseases simultaneously. The one with the reaction developed a sore within a month and secondary signs within 2 months. The other developed no primary sore but secondary signs appeared after 4 months, though as no serological tests were performed before this it is not known exactly at what period the blood

became positive. It is concluded that it is a safe precaution to subject all patients displaying a febrile reaction while under penicillin therapy for gonorrhoea to a clinical and serological scrutiny for 4 months after treatment.

[As mild fever may be missed in patients treated at home, it would be safer to adopt this regimen for all cases of gonorrhoea treated with penicillin.]

R. R. Willcox

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